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10/527,557	11/25/2005	Carl N. Kraus	015280-474200US	7454

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EXAMINER	
KENNEDY, NICOLETTA	
ART UNIT	PAPER NUMBER
1611	
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09/27/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,557	KRAUS ET AL.	
	Examiner	Art Unit	
	Nicoletta Kennedy	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/28/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 14-27 are currently pending.

Priority

This application, filed March 10, 2005, is a national stage entry of PCT/US03/28889, filed September 12, 2003 and claims priority to provisional application 60/410,601, filed September 12, 2002. The instant claims are supported by the provisional application.

Withdrawn Claim Rejections

1. The rejection of claims 28-29 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is obviated by Applicant's cancellation of the claims.

2. The rejection of claims 28-29 under 35 U.S.C. 101 is obviated by Applicant's cancellation of the claims.

New Claim Rejections Necessitated by IDS

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claim 14 is rejected under 35 U.S.C. 102(e) as being anticipated by Rose et al. (US 6,316,433) (filed Dec. 15, 1999).

The claims are directed to a method of inhibiting the growth of *Mycobacterium tuberculosis* comprising administering capreomycin into gases to be inhaled by a patient in need thereof.

Regarding claim 14, Rose et al. claim a method for the treatment of infections caused by *Mycobacterium tuberculosis* comprising inhalation of a combination of rifalazil and capreomycin (claims 1, 6-7 and 14-15).

Therefore, Rose et al. anticipate claim 14.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 15-16 and 18-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rose et al. (US 6,316,433) (filed Dec. 15, 1999) and Montgomery et al. (US 6,387,886) (pub. May 14, 2002).

The claims are directed to a method of inhibiting the growth of *Mycobacterium tuberculosis* comprising administering capreomycin into gases to be inhaled by a patient in need thereof.

Regarding claim 14, Rose et al. claim a method for the treatment of infections caused by *Mycobacterium tuberculosis* comprising inhalation of a combination of rifalazil and capreomycin (claims 1, 6-7 and 14-15). However, Rose et al. fail to teach further details as to the type of formulation. Montgomery et al. cure these deficiencies.

Regarding claim 15, Montgomery et al. teach a method for the treatment of severe chronic bronchitis comprising using a concentrated aminoglycoside formulation (abstract). The aminoglycosides used in the invention include streptomycin, (column 6, line 1), an aminoglycoside also taught to be useful in treating *Mycobacterium tuberculosis* by Staveski et al. (column 9, line 63). The aminoglycoside may be used in powder form (column 6, lines 55-64).

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to have combined the teachings of Rose et al. with those of Montgomery et al. to introduce a powder form of capreomycin into the inhaler. One would have been motivated to do so because Montgomery et al. teach the powder form of aminoglycosides, of which capreomycin is a species. Further, Montgomery et al. teach that streptomycin may be used this way and Rose et al. claim that either capreomycin or streptomycin may be used to treat *Mycobacterium tuberculosis* (claim 7). It would have been within the purview of a skilled artisan to substitute capreomycin for streptomycin because Rose et al. teach that each are known to be used to treat *Mycobacterium tuberculosis*. Further, Montgomery et al. teach that the nebulized particles reach the alveoli (lower lungs), a common goal in treating *Mycobacterium tuberculosis*.

Regarding claim 16, Montgomery et al. teach that the aminoglycoside is in an aerosol or dry powder form and has a mass medium diameter between and 1 and 5 microns (abstract). MPEP 2144.05 states that "[i]n the case where the claimed ranges 'overlap or lie inside ranges disclosed by the prior art' a *prima facie* case of obviousness exists" quoting *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976). In the instant case, the claimed range overlaps the range disclosed by the prior art and is therefore prima facie obvious.

Regarding claims 20 and 24, the above rejection applies. Further, Montgomery et al. teach that the aminoglycoside may be aerosolized (column 5, lines 3-4). One of ordinary skill in the art would reasonably conclude that Rose et al.'s and Montgomery et

al.'s effect of administering a formulation also possesses the same structural and functional properties as those of the effect of administering a formulation claimed and, therefore, it appears that Staveski et al., Capreomycin and Montgomery et al. have produced an effect of administering a formulation to a person that is identical to the effect of administering a formulation to a person. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed method and results thereof with the method and results thereof of Staveski et al., Capreomycin and Montgomery et al., the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the effect of administering a formulation and the effect of administering a formulation of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Regarding claims 18, 21-22, 25-26 and 28, Montgomery et al. teach that the aminoglycoside may be used in a dry powder inhaler, metered dose inhaler, or nebulizer (column 8, lines 46-47 and column 13, line 64).

Regarding claims 19, 23, 27 and 29, Montgomery et al. teach that the aminoglycoside may be used in a jet or ultrasonic nebulizer (column 13, line 65 to column 14, line 5).

Maintained Rejections

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. The rejection of claim 14 under 35 U.S.C. 103(a) as being unpatentable over Staveski et al. (US 6,372,752) (pub. Apr. 16, 2002) in view of Capreomycin (Drug Facts and Comparisons) (pub. 2002) is maintained.

Regarding claim 14, Staveski et al. teach compounds which inhibit the mycobacterial enoyl-ACP reductase required for cell wall biosynthesis, thus inhibiting growth (abstract). The compounds are used in pharmaceutical compositions for treating

a bacterial infection in a patient (abstract). When the bacterial infection is by *Mycobacterium tuberculosis*, capreomycin can be administered as it is a known compound for the treatment of tuberculosis (column 9, lines 55-66). The capreomycin may be administered by inhalation and is introduced with a suitable propellant or other suitable gas (column 11, lines 39-45). However, Staveski et al. fail to teach that capreomycin also prohibits *Mycobacterium tuberculosis* growth. Capreomycin cures this deficiency.

Capreomycin teaches that capreomycin is intended for use with other antitubercolous agents in pulmonary infections caused by capreomycin-susceptible strains of *Mycobacterium tuberculosis* (p. 1494).

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to have combined the teachings of Staveski et al. with those of Capreomycin to administer capreomycin to inhibit growth of *Mycobacterium tuberculosis*. One would have been motivated to do so because Staveski et al. suggest that capreomycin be administered along with the compounds of Staveski et al.'s invention to treat a bacterial infection of *Mycobacterium tuberculosis* and Capreomycin teaches that capreomycin is administered concomitantly with other antituberculous agents to treat capreomycin-susceptible strains of *Mycobacterium tuberculosis*. It is presumed that treatment, read in view of Staveski et al., means inhibit the mycobacterial enoyl-ACP reductase required for cell wall biosynthesis, thus inhibiting growth (abstract).

Response to Arguments

13. Applicant's arguments filed June 28, 2010 have been fully considered but they are not persuasive.

Applicant argues that Staveski only teaches the inhalation of the compounds of Staveski, and not of capreomycin. The examiner respectfully disagrees. Staveski teaches that "for administration by inhalation, the compounds for use according to the present invention are conveniently delivered in the form of an aerosol spray presentation form..." (column 11, lines 39-45). Staveski further teaches that the compounds of the invention can be administered with one or more additional therapeutic agents, including capreomycin (column 9, lines 39-54). Therefore, Staveski suggests the combination of a compound of their invention with capreomycin and administered via inhalation.

Applicant also argues that there is no reasonable expectation of success (remarks, p. 5). However, this is unsupported by evidence. Applicant relies on the Capreomycin reference teaching IV or IM administration and teaching side effects. However, side effects are an unfortunate reality in the field of pharmaceuticals are present in nearly all drugs. Knowledge, management and weighing of the side effects as compared to the benefits of a drug are common. Further, given the dosage information in Capreomycin, it would have been within the purview of one of ordinary skill in the art to determine the safety of inhalation of capreomycin.

With regard to the "unexpected results," no quantitative data has been provided to show the advantages of the instant invention over that of Staveski, the closest prior art.

Therefore, the rejections are maintained.

14. The rejection of claims 15-29 under 35 U.S.C. 103(a) as being unpatentable over Staveski et al. (US 6,372,752) (pub. Apr. 16, 2002) in view of Capreomycin (Drug Facts and Comparisons) (pub. 2002) as applied to claim 14 above, and further in view of Montgomery et al. (US 6,387,886) (pub. May 14, 2002) is maintained.

The combination of Staveski et al. and Capreomycin teach each limitation of claim 14 but fails to teach further detail regarding capreomycin in the formulation. Montgomery et al. cure this deficiency.

Regarding claim 15, Montgomery et al. teach a method for the treatment of severe chronic bronchitis comprising using a concentrated aminoglycoside formulation (abstract). The aminoglycosides used in the invention include streptomycin, (column 6, line 1), an aminoglycoside also taught to be useful in treating *Mycobacterium tuberculosis* by Staveski et al. (column 9, line 63). The aminoglycoside may be used in powder form (column 6, lines 55-64).

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to have combined the teachings of Staveski et al. and Capreomycin with those of Montgomery et al. to introduce a powder form of capreomycin into the inhaler. One would have been motivated to do so because

Montgomery et al. teach the powder form of aminoglycosides, of which capreomycin is a species. Further, Montgomery et al. teach that streptomycin may be used this way and Staveski et al. teach that either capreomycin or streptomycin may be used to treat *Mycobacterium tuberculosis*. It would have been within the purview of a skilled artisan to substitute capreomycin for streptomycin because Staveski et al. teach that each are known to be used to treat *Mycobacterium tuberculosis*. Further, Montgomery et al. teach that the nebulized particles reach the alveoli (lower lungs), a common goal in treating *Mycobacterium tuberculosis*.

Regarding claim 16, Montgomery et al. teach that the aminoglycoside is in an aerosol or dry powder form and has a mass medium diameter bewteen and 1 and 5 microns (abstract). MPEP 2144.05 states that "[i]n the case where the claimed ranges 'overlap or lie inside ranges disclosed by the prior art' a *prima facie* case of obviousness exists" quoting *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976). In the instant case, the claimed range overlaps the range disclosed by the prior art and is therefore prima facie obvious.

Regarding claim 17, Staveski et al. teach that for administration by inhalation, a suitable powder base such as starch, a polysaccharide, is used (column 11, lines 39-50).

Regarding claim 20, Staveski et al. teach compounds which inhibit the mycobacterial enoyl-ACP reductase required for cell wall biosynthesis, thus inhibiting growth (abstract). The compounds are used in pharmaceutical compositions for treating a bacterial infection in a patient (abstract). When the bacterial infection is by

Mycobacterium tuberculosis, capreomycin can be administered as it is a known compound for the treatment of tuberculosis (column 9, lines 55-66). The capreomycin may be administered by inhalation and is introduced with a suitable propellant or other suitable gas (column 11, lines 39-45). Capreomycin teaches that capreomycin is intended for use with other antitubercolous agents in pulmonary infections caused by capreomycin-susceptible strains of *Mycobacterium tuberculosis* (p. 1494). Montgomery et al. teach that the aminoglycoside may be aerosolized (column 5, lines 3-4).

Regarding claim 24, Staveski et al. teach compounds which inhibit the mycobacterial enoyl-ACP reductase required for cell wall biosynthesis, thus inhibiting growth (abstract). The compounds are used in pharmaceutical compositions for treating a bacterial infection in a patient (abstract). When the bacterial infection is by *Mycobacterium tuberculosis*, capreomycin can be administered as it is a known compound for the treatment of tuberculosis (column 9, lines 55-66). The capreomycin may be administered by inhalation and is introduced with a suitable propellant or other suitable gas (column 11, lines 39-45). Capreomycin teaches that capreomycin is intended for use with other antitubercolous agents in pulmonary infections caused by capreomycin-susceptible strains of *Mycobacterium tuberculosis* (p. 1494). Montgomery et al. teach that the aminoglycoside may be aerosolized (column 5, lines 3-4).

Therefore, it is the Examiner's position that the combination of Staveski et al., Capreomycin and Montgomery et al. have produced an aerosolized capreomycin formulation that would reduce the infectivity of the person to whom the formulation is administered. One of ordinary skill in the art would reasonably conclude that Staveski

et al., Capreomycin and Montgomery et al.'s effect of administering a formulation also possesses the same structural and functional properties as those of the effect of administering a formulation claimed and, therefore, it appears that Staveski et al., Capreomycin and Montgomery et al. have produced an effect of administering a formulation to a person that is identical to the effect of administering a formulation to a person. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed method and results thereof with the method and results thereof of Staveski et al., Capreomycin and Montgomery et al., the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the effect of administering a formulation and the effect of administering a formulation of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Regarding claims 18, 21-22, 25-26 and 28, Montgomery et al. teach that the aminoglycoside may be used in a dry powder inhaler, metered dose inhaler, or nebulizer (column 8, lines 46-47 and column 13, line 64).

Regarding claims 19, 23, 27 and 29, Montgomery et al. teach that the aminoglycoside may be used in a jet or ultrasonic nebulizer (column 13, line 65 to column 14, line 5).

Response to Arguments

15. Applicant's arguments filed June 28, 2010 have been fully considered but they are not persuasive. The above response to arguments is hereby incorporated. Applicant

argues that because the combination of Staveski et al. and Capreomycin does not render the claims obvious, and because Montgomery et al. fail to remedy the deficiencies of Staveski et al. and Capreomycin, the instant claims are not rendered obvious. Because the rejection of claim 14 based on the combination of Staveski et al. and Capreomycin is maintained, the rejection based on Staveski et al., Capreomycin and Montgomery et al. is maintained.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicoletta Kennedy whose telephone number is (571)270-1343. The examiner can normally be reached on Monday through Friday 11:30 to 8:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Gollamudi Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. K./
Examiner, Art Unit 1611

/Anne R Kubelik/
Primary Examiner, Art Unit 1638